Objective Techniques for Craniofacial Assessment: What Are the Choices?†

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The approach to an individual with unusual facial appearance has traditionally involved a subjective assessment coupled with a few craniofacial measurements. Our ability to describe facial morphology has improved in recent years through the development of new techniques such as computerized tomography, magnetic resonance imaging, ultrasound studies, and stereoscopic imaging. However, the relatively simpler techniques of anthropometry, cephalometry, and photogrammetry, developed prior to the advent of microchips and imaging software, continue to provide unique advantages not afforded by these technically more sophisticated methods. These objective methods should enhance pattern recognition, particularly in rare syndromes, and allow for earlier diagnosis. Am. J. Med. Genet. 70:1–5, 1997. © 1997 Wiley-Liss, Inc.

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INTRODUCTION

Syndrome diagnosis is based on the clinical observation of abnormal body parts and proportions, and unusual appearance. The diagnosis of a syndrome enables the physician to provide the patient and family with treatment options, possible preventative measures, prognosis, and genetic counselling regarding pathogenesis and recurrence risk. Since a clinical impression may be misleading, it should be validated by quantitative criteria and analytical methodology where possible. Therefore, a thorough phenotypic assessment involves not only an impression of the overall "gestalt" of the face at rest and during crying, smiling, and frowning; it also includes detailed measurement of many craniofacial dimensions. Objective quantitation of phenotype, both at one point in time and with increasing age, should lead to earlier syndrome diagnosis and more complete ascertainment. One can then ask which phenotypic traits are evident at birth, which emerge as the child grows older, and which are submerged or extinguished with increasing age.

Normative physical data have been well-defined in the Caucasian population [Hajnis, 1974; Feingold and Bossert, 1974; Farkas, 1981; Roche and Malina, 1983]. Intrauterine norms are also available [Escobar et al., 1988, 1990]. Many measurements relevant to clinical genetics were compiled recently in a handbook [Hall et al., 1989]. Unfortunately, normal data on other racial and ethnic groups are limited [Biasutti, 1959; Faix, 1982; de la Rosa and Toussaint, 1985; Iosub et al., 1985; Goldenberg et al., 1991].

PHOTOGRAMMETRY

Photogrammetry has been used as an aid to anthropometry and direct observation (anthroposcopy) for over 40 years. Photographs can be obtained quickly and provide a permanent record of the patient which can be evaluated. The outlines of a photograph do not move as they are measured, in contrast to the young child. Unfortunately, fewer facial measurements may be taken from a photograph than by direct methods. Measurements from photographs vary with changes in lighting. Errors may occur in head positioning and in defining bony landmarks. Distortion is proportional to the short distance between the camera and the subject, and projection errors may be unacceptably large unless efforts based on knowledge of photogrammetry are made to reduce them. Some of these shortcomings can be circumvented by the use of ratios/indices [Stengel-Rutkowski et al., 1984; Sharland et al., 1993] or angles [Clarren et al., 1987; Frías et al., 1992] rather than of absolute measurements. The few studies of reliability [Stengel-Rutkowski et al., 1984; Tanner and Weiner, 1949; Gavan et al., 1952; Farkas et al., 1980] have tended to compare photogrammetry and anthropometry. A recent thorough review discusses the optical theory of photogrammetry, providing details of system-

†This article is to be read in companion with Farkas and Deutsch [Am J Med Genet 65:1-4, 1996]; Hunter [Am J Med Genet 65:5-12, 1996]; and Allanson and Cole [Am J Med Genet 65:13-20, 1996].

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atic and random errors [DiLiberti and Olson, 1991]. The authors suggest that measurements based on soft-tissue landmarks may be more amenable to photogrammetry, while an anthropometric approach is preferable for dimensions dependent on bony landmarks which are easily palpated but difficult to identify in photographs. The two methods may give results which differ significantly systematically but not randomly, in which case a correction factor could be determined which would make anthropometric and photogrammetric measurements compatible and interchangeable.

Accuracy of measurement of a three-dimensional object from a two-dimensional image can be enhanced by viewing the object from more than one station, e.g., with three separate cameras set up in a convergent mode [Thomas et al., 1989]. The technique of measuring from a distance, or remote-sensing, has, until recently, been the province of the civil engineer, surveyor, or cartographer. Yet it has great potential in craniofacial analysis. The photographic image is digitized, as are a small number of targets surrounding the subject's face, and the four corners of each frame provide control coordinates. These coordinates are then converted into precise locations in object space. The technique described by Thomas et al. [1989], which is capable of accuracy of 1/100th of an inch, has the potential to make phenotypic description more objective. More complex and expensive remote-sensing devices, such as three-dimensional video scanning systems, are capable of recording a million points on the craniofacial surface and may provide a powerful tool in the future.

CEPHALOMETRY

Cephalometry is the second traditional approach to analysis of the craniofacial area. Head radiographs are obtained using a standardized apparatus (cephalometer) in which the X-ray source is in a fixed relationship to the object [McNamara, 1984]. The head is positioned in a head-holder, thereby controlling the desired projection [Broadbent, 1931]. There are many landmarks and planes from which to choose, and normative data have been established [Riolo et al., 1974; Saksena et al., 1987]. This technique has been applied to syndrome diagnosis, to the evaluation of developmental abnormalities [Pruzansky, 1977; Cohen, 1981, 1985; Kreiborg, 1985], and to the quantitation of craniofacial anomalies in utero [Escobar et al., 1993]. Richtsmeier [1987, 1988] has taken cephalometrics a stage further using finite element scaling analysis, which quantifies the difference in size and shape between forms, without reference to any fixed arbitrary registration point or orientation line. The principal drawback of cephalometry, at least for the clinical geneticist, is the inability to use soft-tissue landmarks.

ANTHROPOMETRY

There are several advantages that anthropometry retains over the above two techniques. It is a simple, noninvasive approach, based on direct measurement of surface dimensions, and has minimal equipment costs. The necessary measurement skills are readily obtained with adequate training and practice. Measurement reliability (intraobserver error) and repeatability (interobserver error) are quantifiable and therefore controllable [Ward, 1989; Ward and Jamison, 1991]. This simplicity makes it an ideal clinical tool when time and financial constraints preclude the use of technically more sophisticated methods. Normal databases for a wide variety of craniofacial dimensions are well-established in the Caucasian population, although few racial or ethnic norms are available [Farkas, 1981]. Powerful, multivariate statistical analysis of these quantitative data is possible. Two excellent reviews of the technique are recommended [Garn et al., 1984, 1985].

Unfortunately, the simplicity of this method can be a disadvantage. There is usually only one opportunity to obtain data on a particular individual, and because this method leaves no permanent record other than a list of numbers, any miscalculations, reading errors, and missing values are often permanent. Anthropometry may be performed by individuals with inadequate training or improper instrumentation. In this situation, the chance of error might be considerable, particularly when the technique is used by nonexperts. There are a few studies which document the magnitude of potential error [Ward, 1989; Ward and Jamison, 1991; Hunter, 1996; Harvey et al., 1994]. The lack of standardization in methodology makes comparison between studies difficult. This difficulty may be compounded by the individual anthropometrist's systematic error. Further evaluation of these limitations would be invaluable prior to the widespread application of this technique.

Nonetheless, anthropometry has been utilized in several areas of clinical genetics, including nosology, documentation of human variation, cause and pathogenesis, diagnosis and prognosis, and treatment. Since 1984, more than 30 anthropometric studies have been published, but most employ only a small number of traditional dimensions, with little emphasis on the craniofacial region, and few take advantage of computer-assisted statistical analysis [Meaney and Farrer, 1986].

Anthropometry can be greatly enhanced by the use of pattern profile analysis identical to that applied to cephalometrics and hand radiographs [Frías et al., 1982; Garn et al., 1984, 1985; Butler et al., 1986]. Dimensions are chosen to represent widths, lengths, depths, heights, and circumferences of the head and face, and to evaluate the eyes, ears, nose, and mouth (Fig. 1). By comparing sample individuals to normal populations, standard Z scores can be generated which can illustrate and compare deviation from "normality" (Fig. 2). A low or high Z score identifies craniofacial dimensions most deviant from average. Craniofacial pattern profiles (CFPP) allow comparison between parent and child, or between an individual and a group with known diagnosis. A correlation coefficient provides a single figure as a measure of similarity between any two patterns. A pattern variability index is a standard deviation of Z-scored measurements expressed relative to norms for age and gender [Garn et al., 1985]. It expresses the degree of dysmorphogenesis as a single

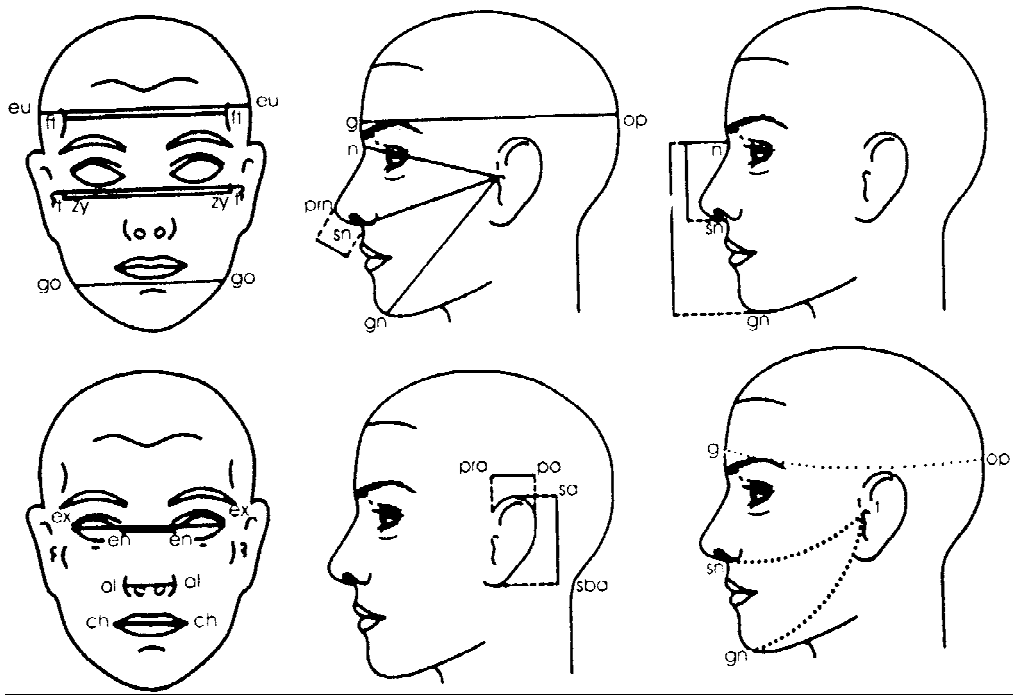

Fig. 1. Dimensions chosen to represent craniofacial widths, lengths, depths, heights, and circumferences, and to evaluate the eyes, ears, nose, and mouth. Reproduced from Allanson and Cole [1996].

number. The more highly patterned an individual, the greater the deviation from the reference population, and the greater the pattern variability index.

Pattern profiles have great potential for improving syndrome recognition and for resolving the similarities and differences between syndromes. The CFPP technique has been used to aid the diagnosis of Wiedemann-Beckwith syndrome [Hunter and Allanson, 1994; Ward et al., 1990], Down syndrome [Allanson et al., 1993], Simpson-Golabi-Behmel syndrome [Hughes-Benzie et al., 1992], and Sotos syndrome [Allanson and Cole, 1996], and for identification of heterozygous fe-

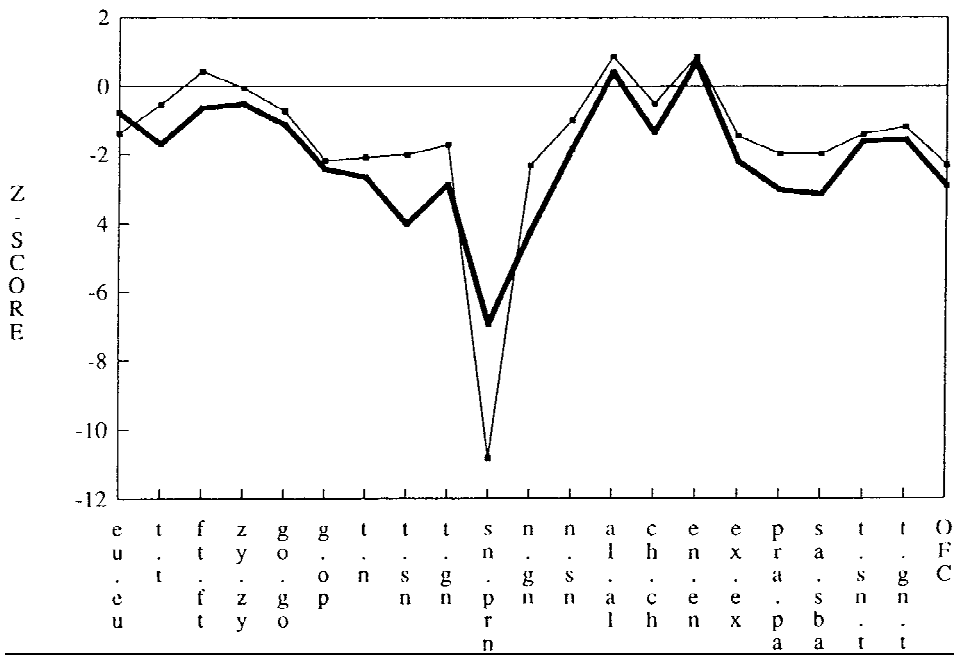

Fig. 2. A craniofacial pattern profile which compares 3-year-old males (fine line) and females (thick line) with Down syndrome. The two patterns are strikingly similar (correlation coefficient, 0.88). The male pattern shows greater variation compared to normal (male pattern variability index, 5.2; female, 2.8).

males with hypohidrotic ectodermal dysplasia [Ward and Bixler, 1987] and Simpson-Golabi-Behmel syndrome [Hughes-Benzie et al., 1992].

The use of anthropometry with CFPP production has important potential in the study of age-related facial changes. The individual structures of the craniofacial complex grow at different rates [Goldstein, 1936; Farkas and Posnick, 1992]. Growth is generally completed first in the head, then in the width of the face, and finally in the length and depth of the face. In both the head and face, vertical dimensions generally increase more than concomitant horizontal dimensions, particularly in males. Acceleration in the rate of growth peaks between age 3–5 years, with some slowing between 5–13 years, and with a secondary peak during puberty. With increasing age and senility most head dimensions are reduced and, except for nasal length, most vertical dimensions of the face decrease. An increase in facial width, with increasing age, is relatively common.

Although the anthropological literature documents different rates of growth in the individual structures of the craniofacial complex, until quite recently awareness of the evolution of facial phenotype in syndromology has been based exclusively on an appreciation of changing "gestalt" [Allanson et al., 1985; Allanson, 1990; Porteous and Goudie, 1991; Fryns, 1992; Lopez-Rangel et al., 1992]. In the last few years, anthropometric studies of this phenomenon have been initiated [Allanson et al., 1993; Hunter and Allanson, 1994; Allanson and Cole, 1996].

CONCLUSIONS

The above discussion of the relative merits of these three techniques is based on the use of traditional craniofacial landmarks, which may have been selected because of their ease of measurement. They may provide a rather inadequate assessment of certain dimensions, e.g., the maximum convexity of the cheek. Computerized three-dimensional shape analysis from a video image, cranial tomography, or a laser scanner may provide equivalent or superior data, both in the normal and in the syndromic face [Clarren et al., 1987; Marsh and Vannier, 1989; Waitzman et al., 1992a,b]. These newer technologies have the potential to revolutionize craniofacial assessment, and deserve extensive evaluation.

The evaluation of the craniofacies in clinical genetics is evolving from a "gestalt" approach to a combination of subjective and objective techniques. Anthropometry, photogrammetry, and cephalometry may be applied alone or in combination to aid definition of syndromic features and thus facilitate diagnosis, document age-related changes, and ultimately assist in the formulation and testing of hypotheses regarding the mechanisms of congenital malformation and deformation.

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